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# Intraoperative Hyperglycemia in Adult Patients Undergoing an Emergency Craniotomy Following a Traumatic Brain Injury as a Predictor of Postoperative Outcomes and Mortality

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INTRAOPERATIVE HYPERGLYCEMIA IN ADULT PATIENTS UNDERGOING AN  
EMERGENCY CRANIOTOMY FOLLOWING A TRAUMATIC BRAIN INJURY AS A  
PREDICTOR OF POSTOPERATIVE OUTCOMES AND MORTALITY

A Research Project submitted to  
the Graduate College of Business  
Marshall University

Final defense submitted in partial fulfillment of requirements for the  
Doctorate of Management Practice in Nurse Anesthesia (DMPNA) degree  
conferred by Marshall University (MU) in partnership with the  
Charleston Area Medical Center (CAMC) based on a collaborative agreement between the  
MU College of Business and the CAMC School of Nurse Anesthesia

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## EXECUTIVE SUMMARY

**Abstract:** The purpose of this study was to determine if there was an association between intraoperative blood glucose  $\geq 150$  mg/dl in patients undergoing an emergency craniotomy and Intensive Care Unit (ICU) Length of Stay (LOS), hospital LOS and mortality.

**Introduction:** Traumatic Brain Injuries (TBI)'s are associated with increased morbidity and mortality. The stress response by the body may cause an increase in blood glucose levels which can cause secondary brain injury. When a patient undergoes an emergency craniotomy following a TBI the increased stress on the body can cause an even higher blood glucose. There is no consensus in the literature as to what level is considered to be hyperglycemic, and there are also no definitive guidelines as to when treatment should be started for rising blood glucose levels. Many studies have found an association between preoperative hyperglycemia and poor postoperative outcomes and mortality, but few studies have looked at intraoperative blood glucose levels with postoperative outcomes and mortality.

**Methodology:** This study used a retrospective, quantitative, case control design at Charleston Area Medical Center in West Virginia. The chart review was conducted on adult patients who presented to the operating room for an emergency craniotomy following a TBI from January 1, 2005 through June 1, 2013. The sample was grouped by the first intraoperative blood glucose, the control group was  $< 150$  mg/dl ( $n=72$ ), and the case group was  $\geq 150$  mg/dl ( $n=47$ ). Patient characteristics of age, gender, Body Mass Index (BMI), mechanism of injury (penetrating or blunt), Injury Severity Score (ISS), intraoperative blood glucose, hospital LOS, ICU LOS, and mortality were collected. Means were compared using the Independent t-test for age, BMI, and ISS. Chi-square test was used to compare gender, ASA physical status, and mechanism of injury. With case control groups a logistic regression was used to determine a relationship between mortality with age, gender, BMI, ISS, mechanism of injury, and intraoperative hyperglycemia. Separate linear regressions analyzed ICU LOS and hospital LOS with age, gender, BMI, ISS, mechanism of injury, and intraoperative hyperglycemia.

**Results:** It was found statistically significant in the mean difference between the two groups (intraoperative blood glucose  $< 150$  mg/dl and  $\geq 150$  mg/dl) in percentage of mortality (5.6% and 21.3%). The mean age of the group was 36.8, mean days in the ICU was 8, mean ISS 28.4, mean days in the hospital 13.9, and mean BMI 26.4. Of the 119 patients, 96 (80.7%) were male, 23 (19.3%) were female, 110 (92.4%) had blunt injury type, 9 (7.6%) had penetrating injury type, and mortality rate was 14 (11.8%). The Odds Ratio showed that the case group was 4.6 times more likely to die compared to the control group which was statistical significant. Statistical significance also was found with age and intraoperative glucose with mortality. ISS association with hospital LOS was shown to be statistically significant. No statistical significance was found between ICU LOS and intraoperative blood glucose.

**Discussion:** This study found that intraoperative blood glucose  $\geq 150$  mg/dl increased the rate of mortality by 4.6 times. Increased age was also shown to have an association with mortality. Increased hospital LOS was associated with ISS. ICU LOS was not shown to be associated with any of the variables tested. The literature has shown that higher glucose levels, age, and ISS have been associated with increase hospital LOS, ICU LOS, and mortality. Several study limitations were identified and discussed.

**Conclusion:** Intraoperative blood glucose  $\geq 150$  mg/dl was associated with a higher rate of mortality.

**Implications/Recommendations:** This study can be used as a guideline to practitioners to use  $\geq 150$  mg/dl as a definition for hyperglycemia in the intraoperative period in emergency craniotomy patients following a TBI to increase the rate of survival.

**Key Words:** traumatic brain injury, hyperglycemia, emergency craniotomy, length of stay, mortality

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## INTRODUCTION

### *Background and Significance*

A craniotomy is a surgical procedure performed when there is a tumor or bleeding in the brain. This is diagnosed by a computed tomography, and the lesion is removed by making an opening in the skull to relieve pressure (Morgan, Mikhail & Murray, 2006). There are many risks associated with a craniotomy including bleeding, blood clots, and swelling which could all cause neurological damage such as nerve tissue damage, loss of brain function, or death (Jaffe & Samuels, 2009). Surgery must be performed to control bleeding, remove hematomas, debride the wound, and remove bone fragments, foreign material, and damaged brain so the cranial vault can better accommodate any swelling that may occur (Sakamoto, Shuer, & Chang, 2006).

A Traumatic Brain Injury (TBI) is the leading cause of death in people less than 24 years of age (Jaffe & Samuels, 2009). An emergency craniotomy may be performed after a TBI. A TBI can be caused from blunt force to the head or can be penetrating into the brain, and can range from mild to severe (Sakamoto et al., 2006). The Centers for Disease Control and Prevention (CDC) have estimated 1.7 million TBI's every year in the United States (U.S.) that have been either isolated events or occurred with other injuries, and both can cause permanent neurological disability and death (CDC, 2013).

Morbidity and mortality have been predicted by preoperative blood glucose levels in trauma patients (Bochicchio, Salzano, Joshi, Bochicchio, & Scalea, 2005; Chabok, Dafchahi, Mohammadi, & Shabbidar, 2009). It has been well researched that hyperglycemia in a critically ill patient is associated with an increase in poor clinical outcomes including neurological function (Lui-Deryke et al., 2009; Marion, 2009). There are conflicting reasons to why blood glucose levels increase in this patient population. It is debatable if the increasing blood glucose

causes poorer outcomes, or if the critically ill patient causes the rise in blood glucose (Chabok et al., 2009; Olsen et al., 2010). The intense stress on the body by the TBI may lead to increasing levels of catecholamines by the sympathoadrenomedullary neuroendocrine response causing hyperglycemia by increased gluconeogenesis. This hypermetabolic stress response may cause metabolic acidosis resulting neuronal cell death in the brain (Lipshutz & Gropper, 2009; Vanhorebeek, Lanjouhe, & Van den Berghe, 2007).

There is a lack of consensus of what defines hyperglycemia. Various blood glucose levels have been used by anesthesia practitioners and researchers to determine the postoperative outcomes of trauma patients with no formal recommendation as to what is an ideal glucose range (Broderick et al., 2007; Bower et al., 2010). There is also controversy if elevated blood glucose levels should be treated with insulin and at what blood glucose level (Bilotta et al., 2007; Bilotta, Caramia, Paoloni, Delfini, & Rosa, 2009). Some blood glucose level ranges offer more conservative therapy where others require a significantly higher blood glucose level before treatment is needed (Bilotta et al., 2008; Meier et al., 2008). Therefore, it is unclear what blood glucose range in the preoperative and intraoperative period is beneficial for postoperative outcomes.

TBI's have been associated with a high morbidity and mortality (Marion, 2009; National Trauma Data Bank, 2012). Secondary brain injury, in TBI patients, can be caused by hypotension, increased intracranial pressure, hypoxia and hyperglycemia (Prisco, Iscra, Ganau, & Berlot, 2012). As preoperative blood glucose has been used as a strong predictor for morbidity and mortality, there is little research on the significance of intraoperative blood glucose levels and postoperative outcomes (Bochicchio et al., 2005). Patients presenting to the operating room for an emergency craniotomy presents a more difficult scenario. Hyperglycemia may already



exist due to the trauma the body has sustained; surgery and anesthetics also stimulate the stress response causing a greater increase in blood glucose levels. This added stress and blood glucose contributes to poorer outcomes (Bilotta et al., 2009; Vanhorebeek et al., 2007).

### *Literature Review*

Many studies have found a relationship between hyperglycemia and poor patient outcomes in patients with a TBI. Most studies have examined preoperative or admission blood glucose (Asilioglu et al., 2011; Prisco et al., 2012). Pecha et al. (2011) conducted a retrospective study on intraoperative blood glucose levels during a craniotomy for TBI. Hyperglycemia was defined as  $\geq 200$  mg/dl and 185 patients were included in the study. It was found that 15 % of patients had intraoperative hyperglycemia and the levels of blood glucose corresponded with the severity of the TBI. There was a 31% mortality rate in those with intraoperative hyperglycemia compared to 13% of those without. If hyperglycemia was defined as 150 mg/dl then 45% would have been considered hyperglycemic. Patients who received insulin for treatment had lower mortality rates, but this study could not define an ideal treatment threshold (Pecha et al., 2011).

Data from 918 consecutive neurosurgical cases was collected by Davis, Ziewacz, Sullivan, & El-Sayed (2012). Preoperative blood glucose levels  $> 100$  mg/dl were associated with increased complication rates compared with levels  $< 100$  mg/dl in a dose response association. Blood glucose levels 121-160 mg/dl and  $> 160$  mg/dl were related to longer Intensive Care Unit (ICU) and hospital Length of Stay (LOS), but levels 100-120 mg/dl were not related to longer ICU and hospital LOS. The authors suggested to have tight blood glucose control  $\leq 120$  mg/dl in patients undergoing a craniotomy (Davis et al., 2012).

Patients who were admitted to the ICU with a TBI had the morning blood glucose levels measured for ten days in a study by Griesdale, Tremblay, McEwen, & Chittock, (2009). There

were a total of 170 patients who included in the study and it was discovered that any hyperglycemic event, with hyperglycemia defined as 200 mg/dl, increased the risk of mortality by 3.6 times. However, there was no association between mean morning blood glucose levels and mortality. It was recommended to keep blood glucose levels  $\leq 180$  mg/dl (Griesdale et al., 2009). Persistent hyperglycemia after a severe TBI was evaluated in a similar study by Salim et al. (2009). There were 105 patients, out of 834, who developed persistent hyperglycemia within the first week of admittance. Whether patients had been treated with insulin or not it was evident that persistent hyperglycemia, defined as a daily glucose average of  $\geq 150$  mg/dl, was associated with an increased risk of morbidity and mortality (Salim et al., 2009).

It is controversial to treat increased blood glucose levels with insulin and at what level should treatment be initiated. It has been suggested that moderate hyperglycemia should be left untreated after a TBI since the blood glucose may be only energy source available and its utilization may be increased to meet the increasing energy demands (Hopwood, Parkin, Bezzina, Boutelle, & Strong, 2005; Parkin et al., 2005). Results from a study by Lui-DeRyke et al. (2009) recommend that the first 24 hours after admission offered a critical time frame where interventions may have the best clinical impact, and to maintain blood glucose levels  $\leq 160$  mg/dl. In a prospective, randomized, controlled study of 1548 critically ill patients, it was found that tight blood glucose control between levels of 80-110 mg/dl with insulin therapy showed decreased morbidity and mortality than convention treatment with insulin if levels were  $\geq 215$  mg/dl (Van den Berghe et al., 2009).

In a retrospective cohort study done by Sharma et al. (2009) perioperative blood glucose (preoperative, intraoperative, and postoperative) levels were evaluated in 105 children who underwent an emergency craniotomy for TBI. There were 47 children (45%) who developed

hyperglycemia, which was defined as blood glucose  $\geq 200$  mg/dl. Very few children were treated with insulin and hyperglycemia was found to be an independent predictor of mortality as 12 of the 15 children who died had hyperglycemia perioperatively, and 7 children had persistent hyperglycemia. Children less than 4 years also showed an increased risk in mortality suggesting that the relationship between hyperglycemia and younger children might show that hyperglycemia can be a cause for poorer outcomes in younger children with a TBI (Sharma et al., 2009). In another study involving 65 children with a TBI, admission hyperglycemia was associated with mortality, trauma severity, and poorer outcomes post discharge. Insulin treatment was started at blood glucose  $\geq 180$  mg/dl (Asilioglu et al., 2011). When Melo et al. (2010) performed a retrospective analysis, mortality was increased by five times with hyperglycemia on admission in children with severe TBI. Out of the 286 children who were included in this study, 98 (34%) were considered hyperglycemic with blood glucose levels  $\geq 200$  mg/dl. There was a 33% mortality rate among the children who were hyperglycemic versus 14% in the normoglycemic children, and there were improved outcomes in patients whose hyperglycemia was treated (Melo et al., 2010). There is no suggestion as to what treatment should be given to children with hyperglycemia and when treatment should be started as there is a risk for increased neurological damage if hypoglycemia would occur after treatment (Van den Berghe et al., 2009).

#### *Statement of the Problem and Research Purpose*

It has been well researched that there is a relationship between hyperglycemia and poor postoperative outcomes and mortality rates. There is a lack of consensus as to what defines hyperglycemia and when to start treating. Previous studies have used levels as high as  $\geq 220$  mg/dl to define hyperglycemia, while others began treatment at  $\geq 110$  mg/dl. Most studies have examined the relationship of postoperative outcomes with preoperative hyperglycemia, while

very few have evaluated intraoperative hyperglycemia. Further research is needed to determine a relationship between intraoperative blood glucose levels and postoperative outcomes and mortality in patients undergoing an emergency craniotomy following a TBI. This could improve clinical practice and patient outcomes at Charleston Area Medical Center (CAMC) in West Virginia and other hospitals where neurosurgery cases are being performed. The importance of this research study was to determine if intraoperative blood glucose levels  $\geq 150$  mg/dl can be used as a predictor for longer ICU LOS, longer hospital LOS, and mortality in this patient population.

The purpose of this study was to examine the relationship between intraoperative blood glucose levels in patients undergoing an emergency craniotomy from a TBI, and postoperative ICU length of stay, hospital length of stay, and mortality.

## METHODOLOGY

### *Research Hypothesis*

The working hypothesis for this study was that patients who have undergone an emergency craniotomy following a TBI with intraoperative blood glucose levels  $\geq 150$  mg/dl will have an increased ICU LOS, hospital LOS, and higher rate of mortality than patients with blood glucose  $<150$  mg/dl.

### *Research Design and Setting*

This research study used a retrospective, quantitative, case control design. This research design was chosen because data could be collected from the trauma registry at the CAMC where patient records could be accessed (West Virginia Department of Health and Human Services, 2013). This case control design allowed identification of patient demographics and

characteristics that could compare intraoperative hyperglycemia and postoperative outcomes including ICU LOS, hospital LOS, and mortality in trauma patients undergoing an emergency craniotomy post TBI.

CAMC is a non-profit, 893 bed academic medical center and regional referral center with four hospitals (CAMC, 2013a). There are three hospitals located in Charleston, West Virginia: General, Memorial, and Women & Children's. The fourth hospital, Teays Valley Hospital, is located in Teays Valley, West Virginia (CAMC, 2013a). The General Hospital serves as a Level I trauma center and has provided trauma services to over 3,000 patients annually (CAMC, 2013b).

A review of medical records was conducted on adult trauma patients who arrived to only CAMC General Hospital requiring an emergency craniotomy after sustaining a TBI from January 1, 2005 through June 1, 2013. Two groups were developed, the control group which were patient's whose first intraoperative blood glucose was  $<150$  mg/dl and the case group who presented as first intraoperative blood glucose  $\geq 150$  mg/dl for comparison of patient demographics and clinical characteristics such as ICU LOS, hospital LOS, and mortality.

#### *Sample Population and Description of Sample*

There was a total of 119 patients selected by statistical randomization with 47 patients having an initial intraoperative blood glucose level  $\geq 150$  mg/dl and 72 patients having an initial intraoperative blood glucose  $< 150$  mg/dl. The subjects were identified by The International Classification of Diseases, 9<sup>th</sup> revision, Clinical Modification (ICD-9-CM) codes 01.21 (craniotomy and craniectomy; incision and drainage of cranial sinus), 01.24-01.25 (other craniotomy, other craniectomy), 800.1-800.4 (fracture of vault of skull closed with cerebral laceration and contusion, closed with subarachnoid, subdural, and extradural hemorrhage, closed

with intracranial injury of other unspecified nature), 800.6-800.9 (fracture of vault of skull open with cerebral laceration and contusion, open with subarachnoid, subdural, and extradural hemorrhage, open with other and unspecified intracranial hemorrhage, open with intracranial injury of other and unspecified nature), 801.1-801.4 (fracture of base of skull closed with cerebral laceration and contusion, closed with subarachnoid, subdural, and extradural hemorrhage, closed with intracranial injury of other unspecified nature), 801.6-801.9 (fracture of base of skull open with cerebral laceration and contusion, open with subarachnoid, subdural, and extradural hemorrhage, open with other and unspecified intracranial hemorrhage, open with intracranial injury of other and unspecified nature), 854 (intracranial injury of other and unspecified nature), and 959.01 (head injury unspecified) were used to identify additional patient subjects included in the study sample (U.S. Department of Health and Human Services, 1989).

Inclusion criteria:

1. Male or female trauma patients.
2. Patients 18 to 64 years of age.
3. American Society of Anesthesiologists (ASA) physical class I-V who underwent an emergency craniotomy following a TBI.
4. An initial or admission blood glucose obtained prior to surgery.
5. At least one blood glucose level obtained during the procedure.

Exclusion criteria:

1. Patients less than 18 years of age or older than 64.
2. Patients with ASA VI.
3. Patients with preexisting diabetes mellitus (DM) defined as pre-existing knowledge of the condition and documented in the history and physical in the patient's chart.

4. No blood glucose level obtained during the procedure.
5. No blood glucose obtained prior to surgery.
6. Patients who had an emergency craniotomy for any other reason than a TBI.

### *Procedures and Protocol*

A retrospective case control study was conducted using patient records from CAMC trauma database who underwent an emergency craniotomy following a TBI. The 119 patients who met the inclusion criteria and had at least one blood glucose level tested during an emergency craniotomy were selected for the study. Patient demographic variables collected from the anesthesia records included: Gender, age, ASA physical status classification, Body Mass Index (BMI), Injury Severity Score (ISS), initial blood glucose level, first intraoperative blood glucose level, mechanism of injury (blunt or penetrating), ICU LOS, hospital LOS, and mortality.

Gender was defined as male or female. Age was measured in years at the time of arrival to the hospital. ASA, which is a subjective assessment given to each patient by the anesthesiologist based on the overall health of the patient was collected. There are six ASA classes: (I) patient is healthy, (II) patient has a mild systemic disease, (III) patient has a non-incapacitating severe systemic disease, (IV) patient has a incapacitating disease that is threatening to life, (V) patient is not expected to live without surgery, and (VI) patient is brain dead and organs are being donated (ASA, 2013). BMI was calculated by a person's weight and height and was used as a predictor for body fat composition (CDC, 2011). The ISS is an anatomical scoring system used when there are multiple parts of the body that have sustained injury. It has been used to predict many measures of severities including mortality and hospital LOS. The Injury Severity Score (ISS) provides a score based on the injury of six body regions (head, face, neck, chest,

abdomen, extremities, and external). An Abbreviated Injury Scale (AIS) was assigned to each injury in each body region, with only the highest AIS in each region used. The AIS uses a six point scaling system from minor (scored 1) to maximal (scored 6). The three highest scores are then squared and added together which determines the ISS (Brohi, 2007).

First intraoperative blood glucose levels referred to the serum specimen obtained either through a venous, arterial, or capillary sample. The first intraoperative sample was the first documented sample in the operating room. Blood glucose was measured in milligrams per deciliter (mg/dl). Mechanism of injury was classified as blunt trauma or penetrating trauma which is injury piercing the skin and causing an open wound (Sung et al., 2005). Hospital LOS and ICU LOS was measured as the number of days that a patient stayed in the hospital and the number of days a patient stayed in the ICU, respectively. Mortality was defined as dead or alive upon discharge from the hospital.

#### *Data Collection and Instrumentation*

Each patient's Electronic Medical Record (EMR) was accessed to obtain data (McKesson Corporation, 2013). Specific data was collected from the emergency room record, anesthesia record, ICU record, records from other nursing units at CAMC where patients received care during the hospital stay, and the CAMC trauma database (West Virginia Department of Health and Human Services, 2013).

The researcher developed a data collection worksheets to organize statistical information. Data Collection Tool 1 was used to assign a study number to each patient. A number was assigned to each patient's record, and the number was unable to be linked back to any patient identification (Appendix A). Data Collection Tool 2 was used to collect and organize patient demographic data including gender, age, ASA physical status classification, BMI, ISS,



admission or initial blood glucose level, first intraoperative blood glucose level, ICU LOS, hospital LOS, and mortality (Appendix B).

### *Statistical Design and Analysis*

The purpose of this research was to examine the relationship between intraoperative blood glucose levels in patients undergoing an emergency craniotomy from a TBI and postoperative outcomes including ICU LOS, hospital LOS, and mortality. The hypothesis for this study was that patients who have undergone an emergency craniotomy following a TBI with intraoperative blood glucose levels  $\geq 150$  mg/dl will have an increased ICU LOS, hospital LOS, and higher rate of mortality than patients with blood glucose  $<150$  mg/dl. The dependent variables included hospital LOS, ICU LOS, and mortality. The main independent variables were the frequency of hyperglycemia in emergency craniotomies identified as blood glucose  $\geq 150$  mg/dl obtained during the intraoperative period, age, gender, BMI, ISS, and injury type. Means were compared using the Independent t-test for the variables of age, BMI, and ISS. Chi-square test was used to compare categorical variables such as gender, ASA physical status, and mechanism of injury. A logistic regression, enter method, was used to determine a relationship between the dependent variable of mortality with the variables age, gender, BMI, ISS, mechanism of injury, and intraoperative hyperglycemia. Separate linear regressions were performed to determine the association between the dependent variables ICU LOS and hospital LOS with the independent variables age, gender, BMI, ISS, mechanism of injury and intraoperative hyperglycemia. A p-value  $<.05$  was considered statistically significant. The data was analyzed using SPSS Version 21 (SPSS IBM Company, 2013).

### *Ethical Considerations*

This study was approved by the Charleston Area Medical Center and West Virginia University-Charleston Division Institutional Review Board on July 25, 2013 (Appendix C).

## RESULTS

### *Presentation, Analysis, and Interpretation of the Data*

The study sample consisted of 119 patients, ages 18-64, presenting to CAMC General Hospital with a TBI who underwent an emergency craniotomy. The mean age of the group was  $36.8 \pm 12.8$ , mean days in the ICU was  $8 \pm 6.2$ , mean ISS  $28.4 \pm 9$ , mean days in the hospital  $13.9 \pm 12.2$ , and mean BMI  $26.4 \pm 4.8$  (Table 1). Of the 119 patients, 96 (80.7%) were male, 23 (19.3%) were female, 110 (92.4%) had blunt injury type, 9 (7.6%) had penetrating injury type, and mortality rate was 14 (11.8%), (Table 1).

Table 1: Clinical Characteristics of Adult Trauma Patients who Underwent an Emergency Craniotomy Following a Traumatic Brain Injury

Variable	Total Sample	Study Groups		Statistical Value
	Total N=119 Mean (SD)	Intraoperative blood glucose < 150 N=72 (60%) Mean (SD)	Intraoperative blood glucose $\geq$ 150 N=47 (40%) Mean (SD)	p-Value
Age (years)	36.8 (12.8)	36.7 (12.8)	36.4 (12.8)	NS
Gender N (%)				
Male	96 (80.7%)	60 (83%)	36 (77%)	NS
Female	23 (19.3%)	12 (17%)	11 (23%)	NS
Blunt Injury Type N (%)	110 (92.4%)	66 (92%)	44 (94%)	NS
Penetrating Injury Type N (%)	9 (7.6%)	6 (8%)	3 (6%)	NS

ISS	28.4 (9)	27.3 (9.3)	29.7 (8.4)	NS
BMI (kg/m <sup>2</sup> )	26.4 (4.8)	25.6 (4.6)	27.7 (4.8)	NS
ICU LOS (days)	8 (6.2)	8.3 (6)	8.2 (6.3)	NS
Mortality (%)	14 (11.8%)	4 (5.6%)	10 (21.3%)	.009*
Hospital LOS (days)	13.9 (12.2)	14.3 (13.2)	13 (10.4)	NS

\*Indicates Statistical Significance at  $p < .05$ , NS= Not Significant ( $p > .05$ ), SD=Standard Deviation, ISS=Injury Severity Score, BMI=Body Mass Index, ICU=Intensive Care Unit, LOS=Length of Stay

The 119 study sample was divided into case control groups according to the first intraoperative blood glucose level obtained with blood glucose  $<150$  mg/dl and  $\geq 150$  mg/dl used for comparison of variables of interest. The control group included 72 (60%) patients with intraoperative blood glucose  $<150$  mg/dl and, the case group included 47(40%) with intraoperative blood glucose  $\geq 150$  mg/dl (Table 1). Comparison between the case control groups did not show age, ISS, BMI, ICU LOS, and hospital LOS as statistically significant ( $p>.05$ ). Statistical significance was found in the mean difference between the two groups in the frequency of mortality with  $p<.05$  (Table 1). The results showed that 4 patients or 5.6% died with an intraoperative blood glucose level  $<150$ mg/dl, while 10 patients or 21.3% died with a blood glucose level  $\geq 150$  mg/dl which was statistically significant ( $p<.05$ ), (Table 1).

A Pearson Chi-Square test was performed between the two groups, and patients from the case group were more likely to die which was statistically significant ( $p<.05$ ), also, the odds ratio showed that patients from the case group showed a 4.59 likelihood to die (Table 2). Mortality

was also associated with intraoperative blood glucose  $\geq 150$  mg/dl as 21.3% of patients in the case group died compared to only 6.3% in the control group ( $p=.009$ ), (Table 2).

Table 2: Analysis of Intraoperative Glucose and Mortality of Adult Trauma Patients who Underwent an Emergency Craniotomy Following a Traumatic Brain Injury

		Mortality		Total
		Dead	Survived	
<150	Count	4	68	72
	Expected Count	8.5	63.5	72
$\geq 150$	Count	10	37	47
	Expected Count	5.5	41.5	47
Total	Count	14	105	119
	Expected Count	14	105	119

#### Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.771	1	.009*		
Continuity Correction	5.341	1	.021		
Likelihood Ratio	6.655	1	.010		
Fisher's Exact Test				.017	.01
N of Valid Cases	339				

#### Risk Estimate

Number of Valid Cases 119	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio ( $\geq 150$ / $<150$ )	4.59	.064	.742
For cohort Dead	.261	.087	.784
For cohort Survived	1.200	1.024	1.406

\*Indicates Statistical Significance at  $p < .05$

Case control groups were analyzed with a logistic regression for the dependent variable mortality with the independent variables of age, gender, BMI, ISS, mechanism of injury, and

intraoperative blood glucose. Statistical significance was found with age and intraoperative glucose with mortality ( $p < .05$ ), (Table 3).

Table 3: Logistic Regression Analysis between Mortality and Adult Trauma Patients who Underwent an Emergency Craniotomy following a Traumatic Brain Injury

	B	S.E.	Wald	df	Sig.
Age	-.054	.026	4.281	1	.039*
Gender	.394	.999	.155	1	NS
BMI	-.053	.068	.617	1	NS
ISS	-.002	.038	.004	1	NS
Injury type	19.044	12580.481	.000	1	NS
Intraoperative Glucose	-1.587	.684	5.377	1	.020*
Constant	6.332	2.281	7.703	1	.006

Dependent Variable: Mortality. \*Indicates Statistical Significance at  $p < .05$ , NS= Not Significant ( $p > .05$ ), BMI=Body Mass Index, ISS=Injury Severity Score

A linear regression, enter method, between the dependent variable ICU LOS with the independent variables age, gender, BMI, ISS, mechanism of injury and intraoperative blood glucose showed no statistical significance ( $p < .05$ ), (Table 4).

Table 4: Linear Regression Analysis between ICU LOS and Adult Trauma Patients who Underwent an Emergency Craniotomy following a Traumatic Brain Injury

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	9.497	4.163		2.281	.024
Age	.036	.046	.075	.791	NS
Gender	-3.033	1.588	-.194	-1.910	NS
BMI	-.172	.133	-.132	-1.291	NS
ISS	.080	.067	.117	1.198	NS
Intraoperative Glucose	.179	1.224	.014	.147	NS
Injury Type	1.225	2.200	.052	.557	NS

Dependent Variable: ICU LOS. \*Indicates Statistical Significance at  $p < .05$ , NS= Not Significant ( $p > .05$ ), BMI=Body Mass Index, ISS=Injury Severity Score

A linear regression, enter method, was conducted with hospital LOS as the dependent variable with the main independent variable intraoperative blood glucose level. The results only showed statistical significance with ISS ( $p < .05$ ). No statistical significance was found with age, gender, BMI, mechanism of injury and intraoperative blood glucose (Table 5).

Table 5: Linear Regression Analysis between Hospital LOS and Adult Trauma Patients who Underwent an Emergency Craniotomy following a Traumatic Brain Injury

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	6.769	7.969		.849	NS
Age	.080	.088	.084	.910	NS
Gender	-3.351	3.040	-.109	-1.102	NS
BMI	-.168	.254	-.066	-.662	NS
ISS	.364	.128	.270	2.845	.005*
Intraoperative Glucose	-2.428	2.344	-.098	-1.036	NS
Injury Type	4.983	4.211	.108	1.183	NS

Dependent Variable: Hospital LOS. \*Indicates Statistical Significance at  $p < .05$ , NS= Not Significant ( $p > .05$ ), BMI=Body Mass Index, ISS=Injury Severity Score

## DISCUSSION

### *Discussion of Study Results*

Other studies have identified hyperglycemia as a predictor for poor postoperative outcomes and mortality in patients with a TBI (Salim et al., 2009; Sharma et al., 2009). This present study has revealed that patients who present to the OR for an emergency craniotomy following a TBI and had the first intraoperative blood glucose level  $\geq 150$  mg/dl were more likely to die which was statistically significant. Increased hospital LOS was associated with ISS as opposed to intraoperative hyperglycemia which was not statistically significant.

There was a greater frequency of males 80.7% which is higher than national trauma statistics which has a frequency of 63% (National Trauma Data Bank, 2012). In 2013, the CDC

also reported that TBI is higher among males than females in every age group. In other similar studies there has been a greater frequency of males (73% and 74.2%) compared to females (Lui-DeRyke et al., 2009; Sung et al., 2005). Males are more engaged in more dangerous activities which make them more susceptible to TBI's including motor vehicle crashes, war, criminal activity, sports, and manual labor (Kennard, 2007).

Increased age was associated with an increase in mortality in the present study. This is consistent with the CDC (2013) which has stated that patients 75 years of age or older accounted for the highest number of TBI related hospitalizations and death. Prisco et al. (2012) stated that age has been described as important predictive factor of mortality in TBI patients, but causes were unclear. The authors proposed that medical complications and preexisting comorbidities could be a reason, or that the intrinsic properties of the ageing central nervous system could delay recovery. Lui-DeRyke et al. (2009) found that the mortality group was significantly older and suggested that could be due to more severe disease. The National Trauma Data Bank (2012) reported that the highest group of fatalities were patients over the age of 75. It was also stated the mean age of a TBI was between 40-50 years old which is higher than the mean found in this study of 36.8 years old.

Mortality was also associated with intraoperative blood glucose  $\geq 150$  mg/dl in patients who had an emergency craniotomy following a TBI in the present study as 21.3% of patients in the hyperglycemic group died compared to only 6.3% in the control group ( $p=.009$ ). This fact was comparable to the literature where hyperglycemia has been associated with higher mortalities for craniotomies (Griesdale et al., 2009; Pecha et al., 2011). When hyperglycemia was defined as 200 mg/dl, 31% of patients with intraoperative hyperglycemia died whereas only 13% of patients who did not have intraoperative hyperglycemia died which was statistically



significant (Pecha et al., 2011). The authors also found that increasing the severity of the TBI, having preoperative hyperglycemia, and increased age were associated with intraoperative hyperglycemia. Griesdale et al. (2009) suggested to keep blood glucose levels  $< 200$  mg/dl for at least 10 days after a TBI to decrease the risk of mortality. Sharma et al. (2009) found that perioperative hyperglycemia in children post TBI had a significantly higher mortality rate using  $\geq 200$  mg/dl as the blood glucose level to define hyperglycemia which was statistically significant. Mortality was more than doubled in trauma patients who required immediate surgical intervention and had a hyperglycemic episode, and there was also an increased ICU LOS and hospital LOS (Bochicchio et al., 2005). This study found that patients who were hyperglycemic in the intraoperative period were 4.6 times more likely to die while using 150 mg/dl to define hyperglycemia. Therefore, using a blood glucose of 150 mg/dl to define hyperglycemia is highly recommended to improve mortality.

Although ISS was not associated with mortality, it was a significant indicator of hospital LOS, but not ICU LOS. Other studies have found a correlation with ISS and mortality and increased hospital LOS and ICU LOS (Davis et al., 2012; Prisco et al., 2012; Salim et al., 2009). Davis et al. (2012) found an increased ICU LOS and hospital LOS with an increase glucose level in a dose-response fashion, and males had an increased hospital LOS, but not ICU LOS. The authors also found no association with age and ICU LOS and hospital LOS, but BMI was associated with an increased ICU LOS, but not hospital LOS. BMI was not significant in the present study or in the literature for emergency craniotomies following a TBI and postoperative outcomes and mortality. Sung et al. (2005) found an increase in hospital LOS and double the risk of mortality with hyperglycemia in critically ill trauma patients.

### *Study Limitations*

This study had several limitations. The patients in this study were from only one institution and does not represent the universal population. There was no power analysis conducted on the sample size, and the sample size may be too small for proper analysis. Although there was inclusion and exclusion criteria, any medications that may have been given in the preoperative or intraoperative period were not accounted for which could have affected the blood glucose levels. These medications could be, but are not limited to, insulin, and dextrose containing solutions, or steroids which could have falsely altered the results. Patients included in the study could have had undiagnosed DM as only a known previous history of DM was an exclusion criteria. Diagnostic lab results were not used to diagnose DM on admission. Other preexisting or undiagnosed co-morbidities could have an impact on the results as DM was the only co-morbidity used in the exclusion criteria. An accurate medical history may not have been able to be obtained from all patients as TBI's may cause confusion, disorientation, or unconsciousness.

Another limitation that may have potentially excluded potential patients from the study is documentation error. Using a retrospective and case controlled design, the data could be misinterpreted or there could be improper documentation. Finally, a cause and effect relationship could not be used to establish causality as it was designed as a retrospective research study.

### CONCLUSION

In the present study, intraoperative hyperglycemia was highly associated with a more likelihood of mortality in patients who underwent an emergency craniotomy following a TBI. Increased

ICU LOS and hospital LOS was not associated with intraoperative hyperglycemia in patients who underwent an emergency craniotomy following a TBI.

### IMPLICATIONS AND RECOMMENDATIONS

This study provides clinical evidence to researchers and practitioners about hyperglycemia in patients who undergo an emergency craniotomy following a TBI regarding more information of the effects of hyperglycemia in postoperative outcomes and mortality. Understanding how hyperglycemia can impact postoperative outcomes and mortality can be detrimental to emergency craniotomies and trauma patients. This valuable information can be helpful for practitioners in the OR to maintain tighter glucose control to improve these outcomes.

This study supports that hyperglycemia in emergency craniotomies following a TBI is associated with an increase in mortality. Hyperglycemia has not been defined by the literature, yet, but in this study blood glucose levels  $\geq 150$  mg/dl was used to define hyperglycemia. It should be recommended to use 150 mg/dl to define hyperglycemia as opposed to higher levels like 200 mg/dl to improve postoperative outcomes and mortality. Further research should be conducted to determine different parameters of blood glucose control in this patient population.

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# APPENDIX A: DATA COLLECTION TOOL 1

Patient Study Number		Patient Identification Number (Acct #)
1		
2		
3		
4		
5		
...		
119		

## APPENDIX B: DATA COLLECTION TOOL 2

Patient Study Number	Gender (M/F)	Age (yrs)	ASA Physical Status (I-V)	BMI (kg/m2)	Admission ISS	Admission Glucose	First Intraoperative Glucose	Presence of Pre-existing Diabetes (Y/N)	Mechanism of Injury (blunt/peircing)	LOS Hospital (Days)	LOS ICU (Days)	Mortality Death or Survived
1												
2												
3												
4												
5												
...												
119												

## APPENDIX C: IRB APPROVAL CERTIFICATE



July 25, 2013

Cassy Taylor, DMP, CRNA  
3110 MacCorkle Avenue SE  
Room 2041  
Charleston, WV 25304

RE: Your application dated 7/11/2013 regarding study number 1997355: INTRAOPERATIVE HYPERGLYCEMIA IN ADULT PATIENTS UNDERGOING AN EMERGENCY CRANIOTOMY FOLLOWING A TRAUMATIC BRAIN INJURY AS A PREDICTOR OF POSTOPERATIVE OUTCOMES AND MORTALITY

Dear Dr. Taylor:

Your request for expedited approval of the new study listed above has been reviewed. This type of study qualifies for expedited review under FDA and DHHS (OHRP) regulations under 5. Materials collected for non research purposes.

This is to confirm your application is approved. The protocol Version 1, July 11, 2013 is approved. The HIPAA Waiver of Authorization signed 7/11/2013 is approved. The data set associated with this study is considered identifiable. The accrual goal of 100 is approved. You must submit a request to the IRB to increase enrollment beyond the approved accrual goal.

You are granted permission to conduct your study as described in your application effective immediately. The study is subject to continuing review on or before 7/25/2014, unless closed before that date.

All investigators and study staff involved with this study must participate in and complete the training, Managing and Reporting Your Study to the IRB, given by the Office of Research and Grants Administration. All parties will be contacted regarding the next scheduled training opportunity.

Please note that any changes to the study as approved must be promptly reported and approved prior to implementation. Some changes may be approved by expedited review; others require full board review. Contact the CAMC/WVU Institutional Review Board office (388-9973; fax 388-9976) if you have any questions or require further information. Your continued cooperation is appreciated.

Sincerely,

John C. Linton, PhD  
Chair, IRB